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1: Science. 1999 May 7;284(5416):974-7.

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- Science. 1999 May 7;284(5416):886.

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Discovery of a small molecule insulin mimetic with antidiabetic activity in mice.

Zhang B, Salituro G, Szalkowski D, Li Z, Zhang Y, Royo I, Vilella D, Diez MT, Pelaez F, Ruby C, Kendall RL, Mao X, Griffin P, Calaycay J, Zierath JR, Heck JV, Smith RG, Moller DE.

Department of Molecular Endocrinology, Merck Research Laboratories, R80W250, Post Office Box 2000, Rahway, NJ 07065, USA. bei_zhang@merck.com

Insulin elicits a spectrum of biological responses by binding to its cell surface receptor. In a screen for small molecules that activate the human insulin receptor tyrosine kinase, a nonpeptidyl fungal metabolite (L-783,281) was identified that acted as an insulin mimetic in several biochemical and cellular assays. The compound was selective for insulin receptor versus insulin-like growth factor I (IGF1) receptor and other receptor tyrosine kinases. Oral administration of L-783,281 to two mouse models of diabetes resulted in significant lowering in blood glucose levels. These results demonstrate the feasibility of discovering novel insulin receptor activators that may lead to new therapies for diabetes.

PMID: 10320380 [PubMed - indexed for MEDLINE]

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